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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/542,427	03/09/2006	Jung-Hyun Kim	54577-10700	3355

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EXAMINER	
FORD, ALLISON M	
ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
11/19/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTO_Mail@hro.com

Office Action Summary	Application No.	Applicant(s)	
	10/542,427	KIM ET AL.	
	Examiner	Art Unit	
	ALLISON M. FORD	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-8 and 10-12* is/are pending in the application.

4a) Of the above claim(s) *1,2,4-7 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,10 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/8/2009 has been entered.

Claims 8, 10 and 11 have been amended; claims 3, 9 and 13-14 have been cancelled. Claims 1, 2, 4-8 and 10-12 remain pending in the instant application, of which claims 1, 2, 4-7 and 12 remain withdrawn from consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected inventions, there being no allowable generic or linking claim. Election was made **without** traverse on 5/7/2008.

Claims 8, 10 and 11 have been considered on the merits.

Priority

Acknowledgment is made that the instant application is a national stage entry under 35 USC 371 of international application PCT/KR04/00054, filed 1/11/2005. Acknowledgement is also made of the instant application claiming foreign priority under 35 USC 119(a)-(d) to Korean application 10-2003-0002314, filed 1/14/2003. A certified copy of the Korean application has been received in the instant application from WIPO.

Oath/Declaration

The substitute declaration received 9/8/2009 is accepted.

Response to Arguments/Amendments

Applicants' remarks, filed 9/8/2009 have been fully considered. Each point will be addressed below, as appropriate. Rejections/objections not repeated herein have been withdrawn.

Please note cancellation of claim 14 has rendered all rejections thereof moot. Furthermore, perfection of the priority claim removes Awad et al (US 2005/0288796) as eligible as prior art, thus rejections previously based on this reference are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Applicants have amended the claims in order to comply with 35 USC 112, second paragraph. The amendments obviate the rejections previously of record; however, the amendments have necessitated the following new grounds of rejection:

Claims 8, 10 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 has been amended to include a step of "gelating a semi-permeable agent on a surface of each of the scaffold pieces .." this steps is found to render the claim indefinite because the meaning of the term "gelating" is unknown. Furthermore, it is unclear if the step of "gelating" is distinct from the previous step of "adding a semi-permeable agent… and a crosslinking agent to the molding container, to form by a cross-linking thereof, a semi-permeable membrane..." It appears both steps require addition of the semi-permeable agent to the molding container to interconnect the scaffold pieces. Clarification is required to distinguish the actions required by each step.

Furthermore, in claim 8, while the preamble states the method is for preparing a biological tissue, the body of the claim never makes it clear that a biological tissue is thereby produced; thus it is unclear if the recited steps effectively achieve the intention set forth in the preamble.

The dependent claims inherit the deficiencies of independent claim 8, and thus are rejected on the same grounds.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Applicants have traversed the rejection under 35 USC 103(a) over Zaleske et al in view of Bouhadir et al on the grounds that Zaleske et al fails to disclose addition of a cross-linking agent, and that the Petri dish does not appropriately read on a molding container having a predetermined form and size and having a morphology of a tissue to be regenerated.

In response to Applicants' argument that Zaleske et al fail to disclose a cross-linking agent, it is respectfully submitted that the rejection is based on the fact that Zaleske et al disclose calcium alginate hydrogel as a species of gel which may be used to coat the cartilage unit (See Zaleske et al, claim 3); and that it was known in the art that calcium alginate gel is formed by combining alginate and calcium chloride (See Bouhadir et al). Therefore, though Zaleske et al does not specifically disclose applying alginate (as the semi-permeable agent) and calcium chloride (as the cross-linking agent) one of ordinary skill in the art would have recognized that both materials would have been necessary for formation of the calcium alginate gel, and thus applied.

In response to Applicants' argument that the Petri dish of Zaleske et al does not read on a molding container as required by the instant invention, as it does not have a morphology of a tissue to be regenerated, it is first respectfully submitted that the claims do not define the morphology of the tissue to be regenerated, thus a container having any form, size and morphology can be considered to 'have a morphology of the tissue to be regenerated'. However, the rejection of record has been modified to address that different molding containers, particularly polytetrafluoroethylene containers, such as the Teflon molds of Bouhadir et al, may have been substituted for the Petri dish in the method of Zaleske et al, thereby addressing all the limitations of the instant claims.

Claims 8, 10 and 11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Zaleske et al (US Patent 6,183,737), in view of Bouhadir et al (Biotechnol Prog. 2001).

Zaleske et al disclose methods of forming a cartilage implant, which reads on the biological tissue as currently claimed. The cartilage implant may be formed by providing two or more non-viable cartilage matrices in apposition, seeding the two or more matrices with isolated chondrocytes to form a cartilage construct, and then applying a biological gel to the cartilage construct to fill gaps at the interface of the two or more cartilage pieces. Alternatively, the individual non-viable cartilage matrices may be seeded with isolated chondrocytes prior to being held in apposition (See Zaleske et al, col. 2, ln 11-33). The cartilage construct may then be implanted *in vivo* (See Zaleske et al, col. 6, ln 16-24).

In their example, Zaleske et al disclose co-culturing chondrocytes with three non-viable cartilage matrices measuring approximately 1 mm in thickness; loading the cell-seeded matrices onto a sterile Petri dish, such that the three matrices are stacked upon one another; applying fibrin glue around the stack of cell-seeded matrices to form a composite cartilage unit; and then implanting the cartilage unit in subcutaneous pockets in nude mice (See Zaleske et al, col. 5, ln 45-col. 6, ln 24).

The non-viable cartilage matrices are considered to read on the scaffolds of the instant invention, thus the step of seeding chondrocytes onto the non-viable cartilage matrices reads on the step of 'seeding cells obtained from a tissue to be regenerated onto one or more scaffolds', it is noted the source of the cells (*i.e.* "from a tissue to be regenerated") is a product-by-process limitation. Process limitations are considered only insofar as the method of production imparts distinct structural or chemical characteristics or properties to the product. In the case of the source of the cells, it is noted that source of the cells does not impart any unique structural characteristics to the cells, thus chondrocytes obtained from any source satisfy the limitation of the current claim.

The step of implanting the cartilage unit *in vivo* is considered to read on the step of introducing nutrients into the scaffold interconnected with the semi-permeable membrane thereby proliferating the tissue cells to produce a biological tissue. Upon implantation *in vivo* the cartilage unit is exposed to nutrients (i.e. blood, growth factors, tissues, etc) in the body; Zaleske et al report that upon recovery the cartilage unit exhibits cellular maturation (See Zaleske et al, col. 8, ln 20-67).

The exemplified method of Zaleske et al differs from the instant invention in that they apply fibrin glue as the biological gel to adhere the cartilage matrices and to fill gaps at the interface(s) between matrices. While the fibrin glue may be considered a semi-permeable agent that forms a semi-permeable membrane on an outer surface of each of the scaffolds, Zaleske et al does not teach further adding a cross-linking agent, as fibrin does not require cross-linking. Zaleske et al further differs from the instant invention in that they utilize Petri dishes as the 'molding container', not polytetrafluoroethylene containers having a predetermined form and size and a morphology of the tissue to be regenerated.

However, given that the level of skill of the artisan in the field of tissue engineering is extremely high, being that of accomplished biomedical engineers, surgeons and cell biologists, usually holding

advanced degrees, it is submitted that the differences between the teachings of Zaleske et al and the current invention would have been found *prima facie* obvious to the artisan of ordinary skill at the time the invention was made based on the knowledge generally available to said artisans and the teachings of the prior art.

With regards to selection of the biological gel, while Zaleske et al exemplify fibrin glue as the biological gel, it is submitted that, at the time the invention was made, it would have been obvious to one of ordinary skill in the art to alternatively use a calcium alginate gel in place of the fibrin glue, as fibrin glue and calcium alginate gel were both disclosed as suitable biological gels which may be used in the method of Zaleske et al (See Zaleske et al, col. 3, ln 63-col. 4, ln 5). Calcium alginate gel is formed by cross-linking alginate with calcium chloride (See, e.g. Bouhadir et al, Pg. 946, col 1 "Hydrogel Formation and Degradation"), thus to use calcium alginate gel as the biological gel, one would apply alginate, and then calcium chloride to the appositioned scaffolds in the method of Zaleske et al. Alginate reads on the 'semi-permeable agent', calcium chloride reads on the cross-linking agent. Suitability of calcium alginate gel for use with chondrocytes and cartilage implants is further supported by Bouhadir et al. Bouhadir et al disclose using calcium alginate gel (formed by cross-linking alginate with calcium chloride) to form substrates for culturing chondrocytes (See Bouhadir et al, Pg. 946, col. 1 "Hydrogel Formation and Degradation"). It has been held that substitution of one element for another known in the field is considered to be obvious, absent a showing that the result of the substitution yields more than predictable results. See *KSR International Co. v Teleflex Inc* 82 USPQ2d 1385 (US 2007) at page 1395. Thus, substitution of calcium alginate gel for fibrin glue as the biological gel in the method of Zaleske et al is held to be *prima facie* obvious.

Furthermore, in using calcium alginate gel as the biological gel in the method of Zaleske et al, it would further have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to utilize a polytetrafluoroethylene mold in place of a Petri dish, based on the teachings of Bouhadir et al. Polytetrafluoroethylene provides a non-stick surface, thus calcium alginate gels are easily removed from polytetrafluorethylene containers without sticking. Bouhadir et al report using Teflon (polytetrafluoroethylene) molding containers to control the shape of the calcium alginate gels (See Bouhadir et al, pg. 946, col. 1). The Teflon molds of Bouhadir et al are considered to read on molding containers having a predetermined form and size, and having a morphology of a tissue to be regenerated, noting that the molds control the form of the calcium alginate semi-solid formed therein. One having ordinary skill in the art would have been motivated to substitute the Teflon (polytetrafluoroethylene) molding containers of Bouhadir et al for the Petri dishes disclosed by Zaleske et al because Teflon containers are non-stick, and thus would ensure easier removal of the tissue construct formed therein.

Furthermore, because the claims do not limit the morphology of the tissue to be regenerated, a tissue construct produced by the prior art method having any shape and size (including that produced from the Teflon molds of Bouhadir et al) may be considered to have a morphology of a tissue to be regenerated. However, even if the morphology of the tissue to be regenerated was limited by the claims (which it currently is not), it is respectfully submitted that Bouhadir et al teach that calcium alginate gels take on the shape of their container, thus, a tissue construct having any desired form, size, and morphology could have been routinely produced by one having ordinary skill in the art by manipulating the size and shape of the Teflon container. Differences in the shape of a product, when the shape would be routinely optimized based on the recognized use/need, are considered to be obvious. See *In re Dailey, 357 F.2d 669, 149 USPQ 47 (CCPA 1966).*

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALLISON M. FORD whose telephone number is (571)272-2936. The examiner can normally be reached on 8:00-6 M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Allison M. Ford/
Primary Examiner, Art Unit 1651